

Docket No.: PF-0334-2 DIV

**REMARKS**

In response to Examiner Roark's suggestions, claims 36 and 39 have been amended. This Supplemental Preliminary Amendment is submitted in compliance with 37 CFR 1.121. Claim 36 now reads, "A method of preparing a polyclonal antibody with the specificity of the antibody of claim 11, the method comprising: . . .". Claim 39 now reads "A method of making a monoclonal antibody with the specificity of the antibody of claim 11, the method comprising: . . .". Applicants expressly state that these claims are **not** being amended for reason related to patentability, and are in fact fully supported by the specification as filed.

By this Supplemental Preliminary Amendment, claims 11, 36-39, 41, and 44 were amended to place the claims in better form for examination and have not been made for reasons relating to patentability. Applicants respectfully request acceptance and entry of this Supplemental Preliminary Amendment.

**Restriction Requirement**

In the Restriction Requirement, the Examiner requested Applicants to elect one of the following inventions:

Group I (claim 1) drawn to a polypeptide comprising SEQ ID NO:1 and variants thereof, classified in Class 435, subclass 183.

Group II (claims 11, 31-32, 34, 36-43) drawn to antibodies to the polypeptide of SEQ ID NO:1, compositions thereof, and methods of making the antibodies, classified in Class 530, subclass 387.1; Class 424, subclass 130.1; and Class 435, subclass 326.

Group III (claims 30 and 44) drawn to a method/diagnostic test for a condition associated with expression of the polypeptide of SEQ ID NO:1, each comprising detecting the polypeptide in a biological sample; classified in Class 436, subclass 63 and Class 435, subclass 7.1.

Group IV (claims 33 and 35) drawn to a method of diagnosing a condition associated with expression of the polypeptide of SEQ ID NO:1 by administering an antibody to the polypeptide to a subject, classified in Class 424, subclass 130.1 and Class 435, subclass 7.1.

Group V (claim 45) drawn to method for using an antibody to purify the polypeptide of SEQ ID NO:1 from a sample; classified in Class 530, subclass 413.

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Applicants hereby elect, with traverse, to prosecute Group II, which includes and is drawn to claims 11, 31-32, 34, and 36-43 drawn to antibodies which specifically bind to polypeptides SEQ ID NO:1, compositions comprising the antibodies, and a method of making antibodies, with traverse.

Claims directed to methods of using the claimed antibodies for diagnosing a condition or disease (i.e., claims 30, 33, and 35), for detecting a polypeptide of SEQ ID NO:1 (i.e., claim 44), and for purifying a polypeptide of SEQ ID NO:1 (i.e., claim 45), could and should be examined together with the product claims from which they depend, per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of one of the product claims, for rejoinder of process claims covering the same scope of products. Applicants presume these method claims will be rejoined, upon determining allowability of the product claims from which they depend.

Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at (650) 621-8555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

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Respectfully submitted,  
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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**  
**IN THE SPECIFICATION:**

**The first paragraph of page 1 has been amended as follows:**

This application is a divisional [of] application of U.S. application serial number 09/258,643 filed on February 26, 1999, now U.S. Patent No. 6,277,373, which is a divisional [of] application of U.S. application serial number 08/884,681 filed on June 27, 1997, now U.S. [patent number] Patent No. 5,955,338, the contents all of which are hereby incorporated by reference.

**IN THE CLAIMS:**

**Claim 1 has been canceled.**

**Claims 11, 36-39, 41, and 44 have been amended as follows:**

11. (Once Amended) An isolated antibody which specifically binds to a polypeptide [of claim 1] selected from the group consisting of:

- a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1,
- b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity,
- c) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.

36. (Once Amended) A method of preparing a polyclonal antibody with the specificity of the antibody of claim 11, the method comprising:

- a) immunizing an animal with a polypeptide having an amino acid sequence of SEQ ID NO:1[,] or an immunogenic fragment thereof, under conditions to elicit an antibody response;
- b) isolating antibodies from said animal; and
- c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having an amino acid sequence of SEQ ID NO:1.

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37. (Once Amended) [An] A polyclonal antibody produced by a method of claim 36.

38. (Once Amended) A composition comprising the polyclonal antibody of claim 37 and a suitable carrier.

39. (Once Amended) A method of making a monoclonal antibody with the specificity of the antibody of claim 11, the method comprising:

- a) immunizing an animal with a polypeptide having an amino acid sequence of SEQ ID NO:1[,] or an immunogenic fragment thereof, under conditions to elicit an antibody response;
- b) isolating antibody producing cells from the animal;
- c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells;
- d) culturing the hybridoma cells; and
- e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having an amino acid sequence of SEQ ID NO:1.

41. (Once Amended) A composition comprising the monoclonal antibody of claim 40 and a suitable carrier.

44. (Once Amended) A method for detecting a polypeptide having an amino acid sequence of SEQ ID NO:1 in a sample, the method comprising [the steps of]:

- a) incubating the antibody of claim 11 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and
- b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having an amino acid sequence of SEQ ID NO:1 in the sample.

[illegible]

**FIGURE 2A**

Inventors: Hillman et al.

Title: PHOSPHATIDYLINOSITOL 4,5-BISPHOSPHATE 5-PHOSPHATASE

Serial No.: 09/892,287

638789  
9 - - - - -  
3 - - - - - g1399105  
236 LQPRQNKSKSEITDMV - RSSTITVSDKAHILS - MQKF - - - g1019103  
173 IHREPPPPFSSVKNKMLPREKEASNKEQPKVTNTMRKLFVP g1420920

638789  
9 - - - - -  
3 - - - - - g1399105  
271 - - - GLRDTIVKSHLLQKEEDYTYIQNFRFFAGTYNVNGQ g1019103  
213 NTQSGQREGLIKHI LAKREKEYVNIQTFRFFVGTWNVNGQ g1420920

638789  
9 - - - - -  
3 - - - - - g1399105  
307 SPKECLR L WLSNGIQAPDVYCVGFQELDL SKEAFFFHDT P g1019103  
253 SPDSGLEPWLNCDPNPPDIYICIGFQELDLSTEAF F FESV g1420920

638789  
9 - - - - -  
3 - - - - - g1399105  
347 KEEWFKA VSEGLHPDAKYAKV K L I R L V G I M L L L Y V K Q E H g1019103  
293 KEQEW S M A V E R G L H S K A K Y K V Q L V R L V G M M L L I F A R K D Q g1420920

638789  
31 L P Y I O I L S T K S T P T G L F G Y W G N K G G V N I C L K L Y G Y V S I I g1399105  
3 - - - - -  
387 A A Y I S E V E A E T V G T G I M G R M G N K G G V A I R F Q F H N T S I C V V g1019103  
333 C R Y I R D I A T E T V G T G I M G K M G N K G G V A V R F V F H N T T F C I V g1420920

638789  
71 N C H L P P H I S N N Y Q R L E H F D R I - L E M O N C E - G R D I P - - N I L g1399105  
3 - - - - -  
427 N S H I A A H I E E Y E R R N Q D Y K D I C S R M Q F Q P D P S L P L T I S g1019103  
373 N S H I A A H V E D F E R R N Q D Y K D I C A R M S F V P N Q T L P Q L N I M g1420920

FIGURE 2B

107	D	H	D	L	I	I	W	F	G	D	M	N	F	R	I	E	D	F	G	L	H	F	V	R	E	S	I	K	N	R	C	Y	G	G	L	W	E	K	D	Q	638789	
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	g1399105			
467	N	H	D	V	I	L	W	L	G	D	L	N	Y	R	I	E	L	D	V	E	K	V	K	K	L	I	E	E	K	D	F	Q	M	L	Y	A	Y	D	Q	g1019103		
413	K	H	E	V	V	I	W	L	G	D	L	N	Y	R	I	E	L	C	M	P	D	A	N	E	V	K	S	L	I	N	K	K	D	L	Q	R	L	K	F	D	Q	g1420920
147	L	S	I	A	K	K	H	D	P	L	L	R	E	F	Q	E	G	R	L	L	F	P	P	T	Y	K	F	D	R	N	S	N	D	Y	D	T	S	E	K	K	638789	
25	L	N	M	A	K	N	T	W	P	I	L	K	G	F	Q	E	G	P	L	N	F	A	P	T	E	K	F	D	V	G	T	N	K	Y	D	T	S	A	K	K	g1399105	
507	L	K	I	Q	V	A	A	K	T	V	F	E	G	F	T	E	G	E	L	T	F	Q	P	T	Y	K	Y	D	T	G	S	D	D	W	D	T	S	E	K	C	g1019103	
453	L	N	I	Q	R	T	Q	K	K	A	F	V	D	E	N	E	G	E	I	K	E	I	P	T	Y	K	Y	D	S	K	T	D	R	W	D	S	S	G	K	C	g1420920	
187	R	K	P	A	W	T	D	R	I	L	W	R	L	K	R	Q	P	C	A	G	P	D	T	P	I	P	P	A	S	H	F	S	L	S	L	R	G	Y	S	S	638789	
65	R	K	P	A	W	T	D	R	I	L	W	K	V	K	-	A	P	G	G	G	E	S	P	S	G	R	K	S	H	R	L	Q	V	T	Q	H	S	Y	R	S	g1399105	
547	R	A	P	A	W	C	D	R	I	L	W	K	G	K	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	g1019103		
493	R	V	P	A	W	C	D	R	I	L	W	R	G	T	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	g1420920		
227	H	M	T	Y	G	I	S	D	H	K	P	V	S	G	T	F	D	L	E	L	K	P	L	V	S	A	P	L	I	V	L	M	P	E	D	L	W	T	V	-	638789	
104	H	M	E	I	T	V	S	D	H	K	P	V	A	A	Q	F	L	Q	F	A	F	R	D	D	M	P	L	V	R	L	E	V	A	D	E	W	V	R	-	g1399105		
570	H	M	A	L	K	T	S	D	H	K	P	V	S	S	V	F	D	I	G	V	R	V	V	N	D	E	L	Y	R	K	T	L	E	E	I	V	R	S	L	D	g1019103	
516	H	M	E	L	K	T	S	D	H	K	P	V	S	A	L	E	H	I	G	V	K	V	V	D	E	R	R	Y	R	K	V	F	E	D	S	V	R	I	M	D	g1420920	
266	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	638789		
143	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	g1399105			
610	K	M	E	N	A	N	I	P	S	V	S	L	S	K	R	R	E	F	C	F	Q	N	V	K	Y	M	Q	L	K	V	E	S	F	T	I	-	H	N	G	Q	V	g1019103
556	R	M	E	N	D	F	L	P	S	L	E	L	S	R	R	E	F	V	F	E	N	V	K	F	R	Q	L	Q	K	G	K	F	Q	I	S	N	N	G	Q	V	g1420920	
300	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	638789		
177	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	g1399105		
649	P	C	H	F	E	F	I	N	K	P	D	E	E	S	Y	C	K	Q	W	L	N	A	N	P	S	R	G	F	L	L	P	D	S	D	V	E	I	D	L	E	g1019103	
596	P	C	H	F	S	F	I	P	K	L	N	D	S	Q	Y	C	K	P	W	L	R	A	E	P	F	E	G	Y	L	E	P	N	E	T	V	D	I	S	L	D	g1420920	

FIGURE 2C



317 LNQVYIDISNIPPTTED [E F] 638789  
192 TYQVTFSEESLPKCHG [D F] g1399105  
689 LFVNKTTATKLNSGEDKIEDILVHLDRGKDYFLSVSGNY g1019103  
636 VYVSKDSVTILNSGEGKIEDILVHLDRGKDYFLTSIGNY g1420920

335 LLYYSNSLSRVVGISRPF-QIP 638789  
210 ILGYYSHNHSLILIGITPEF-QISLPS-SELA SSTDSSGT g1399105  
729 LPSCFGSPIHHTLCLCYMREPI LDLPLETTISEL- - - - - g1019103  
676 LPSCFGTSL EALCRMKRP IREVEVTKLIDLEEDSFLEKEK g1420920

357 - - - - - 638789  
248 S - - - - - SEGEDDSTLE - - - - - LAPKSRSPSPGKSKRRSRSPG g1399105  
759 TLMVWVGDDGSQLDSPMEIPKELWMMVVDYLYRNAVQQED g1019103  
716 SLLQMVPLDEGAS-ERPLQVPKEIWLVDHLFKYACHQED g1420920

357 - - - - - 638789  
282 LARFPGLA - - - - - LRPSRERRRGASRSPSPQSRRLS g1399105  
799 LFQQPGLRSEFEHIRDCLDTSIPEITPGSNHSHVAEALLIF g1019103  
755 LFQTPGMQEEELQIIDCLDTSIPEITPGSNHSHVAEALLIF g1420920

357 - - - - - 638789  
313 RVA - PDRSSNGSSRGSSSEEGPSGLPGPWAFPPAVPRS - - - - - g1399105  
839 LESLPEPVICYSTYHNCLCSCGNYTASQVISTLPFHKN g1019103  
795 LEALPEPVICYELYQRCCLDSAYDPRICRQVISQLPRCHRN g1420920

357 - - - - - [P G] 638789  
349 - - - - - LGLLPAL - RLETVDPGGGSGWGPDRREAL - - - - - APN g1399105  
879 VFHYLMAFLRELKNSAKNHLDENILASIFGSLLLRNPA[G] g1019103  
835 VFHYLMAFLRELKNSAKNHLDENILATLFTSLLLRPP[P]N g1420920

FIGURE 2D